

Neural Disturbances in Chickens Caused by Dietary T-2 Toxin¹

R. D. WYATT, W. M. COLWELL, P. B. HAMILTON, AND H. R. BURMEISTER

Department of Poultry Science and Department of Microbiology, North Carolina State University, Raleigh, North Carolina 27607, and Northern Regional Research Laboratory, Agricultural Research Service, U. S. Department of Agriculture, Peoria, Illinois 61604

Received for publication 23 July 1973

Graded concentrations of dietary T-2 toxin (0, 1, 2, 4, 8, and 16 $\mu\text{g/g}$) were fed to groups of 40 chickens. T-2 toxin was found to cause an abnormal positioning of the wings, hysteroid seizures, and impaired righting reflex in young chickens. The abnormal wing positioning occurred spontaneously or as the result of dropping from a height of 1 meter. The seizures could be elicited by rough handling or loud noises. The seizures and the abnormal wing posture would not occur again when the stimulus was repeated unless a rest period of 3 to 6 h was allowed. The loss of righting reflex could be demonstrated at any time. The total incidence of neural symptoms was dependent on the length of exposure to T-2 toxin and to its concentration. Neural toxicity occurred at dosages of 4, 8, and 16 μg per g of diet, which are the same doses that retard growth. This neural toxicity of T-2 toxin in chickens is similar to the neural disturbances associated with alimentary toxic aleukia, a nutritional toxicosis of humans produced by eating moldy grain. T-2 toxin has been implicated also in moldy corn toxicosis which has neural manifestations in horses and swine.

T-2 toxin [4,15-diacetoxy-8-(3-methylbutyryloxy)-12,13-epoxy- Δ^9 -trichothecen-3-ol] is a mycotoxin originally isolated from a strain of *Fusarium tricinum* which was implicated in moldy corn toxicosis of farm animals (2). Subsequent reports have indicated that T-2 toxin also is produced by other fungi (3, 7). One of the outstanding properties of this toxin is its ability to act as a local irritant (13). Irritation and necroses of the skin have resulted from local application to the skin of rabbits (13), and laboratory workers investigating T-2 toxin have experienced a severe contact dermatitis (2). Dietary T-2 toxin causes oral lesions in chickens (21) resembling those found in the third or septic angina stage of alimentary toxic aleukia (ATA), a nutritional toxicosis of humans which was a major health problem in Russia for two decades (14, 15).

Another trait of T-2 toxin which has received less attention is its influence on the nervous system. It has been implicated in "bean-hulls poisoning" of horses which is characterized by staggering and other disturbances of the nervous system (19). In a thorough survey of T-2

toxin for its toxicological properties in rats, Kosuri et al. (12) found that T-2 caused prolonged pentobarbital and hexobarbital sleeping times and decreased the recovery phase of isolated gastrocnemius muscle preparations without altering the transmission of the applied stimulus. ATA, which generally is thought to be fusariotoxicosis (14) and which bears many similarities to T-2 toxicosis (21), has several features indicating a serious involvement of the nervous system. These features may include impaired reflexes, meningism, dermatographism, hyperesthesia, various neuropsychiatric manifestations, and encephalitic symptoms (9, 14). These functional disorders may be explained by the destructive changes in the neurons of the third ventricle and of the sympathetic ganglia. The general vascular hypotonia and insufficiency which dominate the clinical picture of fully developed ATA are thought to result from the diencephalic changes (14).

In an attempt to gain further information about T-2 toxin and its possible role in moldy corn toxicosis and in ATA, we investigated some of its effects on the nervous system of chickens. The present communication describes some of the neural symptomatology in chickens resulting from graded doses of dietary T-2 toxin.

¹ Paper Number 4122 of the Journal Series of the North Carolina State University Agricultural Experiment Station, Raleigh, N.C.

malities had normal corneal reflexes and their vision was judged to be normal.

DISCUSSION

The unusual array of neural symptoms described here and the previously described oral lesions (21) would appear to be beneficial in the diagnosis of T-2 toxicosis in chickens. To our knowledge these symptoms occur rarely in chickens. Although the righting reflex is lost in chickens with muscular dystrophy (1), the other symptoms appear unique. Despite their rare occurrence, the neural symptoms are not as sensitive and as certain an indicator of T-2 toxicosis in chickens as is the occurrence of oral lesions. Dietary T-2 toxin at levels as low as 1 µg/g will cause characteristic raised yellowish lesions in the mouths of 100% of the birds receiving that level of toxin (21). Even at 16 µg/g, T-2 toxin caused visible neural symptoms in only 37.5% of the birds.

These neural symptoms should aid in an assessment of the role of T-2 toxin in moldy corn toxicosis. Although the toxin was isolated as the result of an investigation of the disease (2, 10), the original description of the disease in chickens (9) does not mention neural symptoms. However, moldy corn toxicosis was reported to cause a staggering gait in swine (9) and a leukoencephalomalacia characterized by liquefaction necrosis of the brain in horses (18). A similar situation exists with the oral lesions caused by T-2 toxin. The original descriptions of moldy corn toxicosis (9, 10) make no mention of oral lesions; however, oral lesions apparently identical to those caused by T-2 toxin have been reported since that time in field cases in chickens and pigeons (20) and in laboratory studies of fusariotoxicosis in turkeys (8) and goslings (17). Additional field cases in which the affected animals are specifically examined for neural symptoms and oral lesions should aid in a more accurate definition of the role of T-2 toxin in moldy corn toxicosis.

The status of ATA is uncertain despite its being a major health concern in Russia for about two decades (14, 15). It is generally accepted that this nutritional toxicosis is caused by the ingestion of grain infected with *Fusarium* sp. (9, 15, 21), although the toxic principle(s) responsible for the disease do not appear to have been isolated (15, 21). Wyatt et al. (21) pointed out many similarities between T-2 toxicosis and ATA, and they suggested that T-2 toxin might be involved in ATA. The present observations on the occurrence of neural disturbances during T-2 toxicosis of chickens

support this suggestion. Although neural disturbances are not obvious in all cases of ATA, there is ample evidence that they are a major underlying problem in severe cases (14). Also, grain that caused ATA in man caused a syndrome in geese characterized by nervous disorders—convulsion-like signs, rigidity, dropping to one side, and ataxia (15). The present observations are in keeping with the symptoms of "bean-hulls poisoning" of horses in which T-2 toxin has been implicated (19), and with the laboratory studies on the toxicology of T-2 toxin in rats (12).

Because *Fusarium* and related fungi produce several other toxins closely related to T-2 toxin (3, 6, 16, 19), it would seem appropriate to investigate them more thoroughly both individually and with regard to their possible interactions. In particular, the neurotoxicity of these fusariotoxins would appear to be interesting and fruitful areas of inquiry. Then, perhaps, the responsibility for ATA and moldy corn toxicosis can be assigned to specific chemical entities, and the current ill-defined status of these important diseases can be dispelled.

ACKNOWLEDGMENTS

We thank Sharon West, G. Whittaker, and Nancy Goodwin for technical assistance.

LITERATURE CITED

1. Albuquerque, E. X., and J. E. Warnick. 1971. Electrophysiological observations in normal and dystrophic chicken muscles. *Science* 172:1260-1263.
2. Bamberg, J. R., N. V. Riggs, and F. M. Strong. 1968. The structures of toxins from two strains of *Fusarium tricinatum*. *Tetrahedron* 24:3329-3336.
3. Bamberg, J. R., and F. M. Strong. 1969. Mycotoxins of the tricothecane family reproduced by *Fusarium tricinatum* and *Trichoderma lignorum*. *Phytochemistry* 8:2405-2410.
4. Bruning, J. L., and B. L. Kintz. 1968. Computational handbook of statistics. Scott Foresman Co., Glenview, Ill.
5. Burmeister, H. R. 1971. T-2 toxin production by *Fusarium tricinatum* on solid substrate. *Appl. Microbiol.* 21:739-742.
6. Burmeister, H. R., J. J. Ellis, and S. G. Yates. 1971. Correlation of biological to chromatographic data for two mycotoxins elaborated by *Fusarium*. *Appl. Microbiol.* 21:673-675.
7. Burmeister, H. R., J. J. Ellis, and C. W. Hesseltine. 1972. Survey for fusaria that elaborate T-2 toxin. *Appl. Microbiol.* 23:1165-1166.
8. Christensen, C. M., R. A. Meronuck, G. H. Nelson, and J. C. Behrens. 1972. Effects on turkey poults of rations containing corn invaded by *Fusarium tricinatum* (Cda.) Syn. & Hans. *Appl. Microbiol.* 23:177-179.
9. Forgacs, J., and W. L. Carll. 1972. Mycotoxicoses. *Advan. Vet. Sci.* 7:273-382.
10. Gilgan, M. W., E. B. Smalley, and F. M. Strong. 1966. Isolation and partial characterization of a toxin from *Fusarium tricinatum* on moldy corn. *Arch. Biochem. Biophys.* 114:1-3.

11. Gowers, W. R. 1964. Epilepsy and other chronic convulsive diseases: their causes, symptoms, and treatment. Dover Publication Inc., New York.
12. Kosuri, N. R., E. B. Smalley, and R. E. Nichols. 1971. Toxicologic studies of *Fusarium tricinctum* (Corda) Snyder et Hansen from moldy corn. Amer. J. Vet. Res. 32:1843-1850.
13. Marasas, W. F. O., J. R. Bamberg, E. B. Smalley, F. M. Strong, W. L. Ragland, and P. E. Degurse. 1969. Toxic effects on trout, rats, and mice of T-2 toxin produced by the fungus *Fusarium tricinctum* (Cd.) Synd. Hans. Toxicol. Appl. Pharmacol. 15:471-482.
14. Mayer, C. F. 1953. Endemic panmyelotoxicosis in the Russian grain belt. I. The clinical aspects of alimentary toxic aleukia (ATA); a comprehensive review. Mil. Surg. 113:173-189.
15. Mayer, C. F. 1953. Endemic panmyelotoxicosis in the Russian grain belt. II. The botany, phytopathology, and toxicology of Russian cereal Food. Mil. Surg. 113:295-315.
16. Mirocha, C. J., C. M. Christensen, and G. H. Nelson. 1968. Toxic metabolites produced by fungi implicated in mycotoxicoses. Biotech. Bioeng. 10:469-482.
17. Palyusik, M., I. Szep, and F. Szoke. 1968. Data on susceptibility to mycotoxins on day-old goslings. Acta Vet. Med. Hung. Tomus 18:363-372.
18. Schwarte, L. H., H. E. Biester, and C. Murray. 1937. A disease of horses caused by feeding moldy corn. J. Amer. Vet. Med. Ass. 90:76-85.
19. Ueno, Y., K. Ishii, K. Sakai, S. Kanaeda, H. Tsunoda, T. Tanaka and M. Enomoto. 1972. Toxicological approaches to the metabolites of Fusaria. IV. Microbial survey on "bean-hulls poisoning of horses" with the isolation of toxic trichothecenes, neosolaniol and T-2 toxin of *Fusarium solani* M-1-1. Jap. J. Exp. Med. 42:187-203.
20. Wyatt, R. D., J. R. Harris, P. B. Hamilton, and H. R. Burmeister. 1972. Possible outbreaks of fusariotoxicosis in avians. Avian Dis. 16:1123-1130.
21. Wyatt, R. D., B. A. Weeks, P. B. Hamilton, and H. R. Burmeister. 1972. Severe oral lesions in chickens caused by ingestion of dietary fusariotoxin T-2. Appl. Microbiol. 24:251-257.

Purchased by Agricultural Research Service, U.S. Dept. of Agriculture, for official use

